Comm.
Dr. Bing
Dr. Cattell
Dr. Meier

PHARMACOLOGY #900

THE COUNCIL FOR TOBACCO RESEARCH–U.S.A., INC.
110 EAST 59TH STREET
NEW YORK, N. Y. 10022
(212) 421-8885

JAN 3 1 1973

Application for Research Grant
(Use extra pages as needed)

Date: Jan.26, 1973

1. Principal Investigator (give title and degrees):

Victor J. Schenker, Ph.D.
Research Professor of Biochemistry

2. Institution & address:

Temple University, School of Dentistry
3223 N. Broad St.
Philadelphia, Pa. 19140

3. Department(s) where research will be done or collaboration provided:

Dept. of Biochemistry, School of Dentistry
Dept. of Pharmacology, School of Pharmacy

4. Short title of study.

Neuroactive Components of Human Saliva and Their Possible Interaction with Nicotine.

5. Proposed starting date: July 1, 1973

6. Estimated time to complete: 2 years.

7. Brief description of specific research aims: Previous work by this investigator shows the presence of neuroactive material in extracts of human saliva having the spectrofluorometric characteristics of biogenic amines related to tyramine. This is also found in homogenates of human submaxillary gland tissue. Preinjection of extracts containing this salivary fluorophore (SF) in mice caused a 2- to 3- fold prolongation of sleeping time due to hexobarbital. This potentiation does not occur when nicotine is added to SF extracts, suggesting a new approach to the study of the relationship between nicotine and neuroactive biogenic amines. Cholinergic stimulation by urecholine in human subjects elicits a marked increase of SF in saliva, in contrast to atropine which is followed by a decrease indicating autonomic mediation of the elaboration and/or release of SF from the salivary glands. Direct application of SF to the right heart in dogs with heart catheterization elicits marked increase in right ventricular pressure and pulmonary circuit. The proposed research is an attempt to elucidate these findings. Specific aims are directed at the precise chemical identification of SF together with its pharmacological and neurochemical characterization in terms of activity at extra-oral sites (e.g., brain, heart) from possible absorption through the oral mucosa, with particular emphasis upon interaction with nicotine similarly absorbed.

8. Brief statement of working hypothesis:

An overall working hypothesis stemming from the combined findings of our previous work has been formulated as follows: 1) human saliva contains one or more neuroactive biogenic amines ostensibly elaborated by and/or released from the submaxillary salivary glands under the mediation or modulation of the autonomic nervous system; 2) such compounds, continuously present in the oral cavity, may be absorbed through the oral mucosa and transported directly to the right heart and, via the pulmonary circuit, reach the brain and other organs before chemical alteration by passage through the hepatic or renal circulation. This vascular shunt could thus facilitate the homeostatic interaction of these compounds with other regulatory factors at extra-oral sites. As a corollary, such interaction may be affected by the presence of exogenous agents (e.g., nicotine) in the oral cavity, from which they are absorbed.

9. Details of experimental design and procedures (append extra pages as necessary)

See appended Research Plan, pp.6 through 21

10. Space and facilities available (when elsewhere than item 2 indicates, state location):

see Research Plan - Section 1-D, page 14

11. Additional facilities required:

none

12. Biographical sketches of investigator(s) and other professional personnel (append): appended ff. page 21

13. Publications: (five most recent and pertinent of investigator(s); append list, and provide reprints if available).

See Section 2-C, pp. 20-21

4.

14. First year budget:

A. Salaries (give names or state "to be recruited") Professional (give % time of investigator(s) even if no salary requested)	% time	Amount
Dr. Victor J. Schenker (Principal Investigator)	60	REDACTED
Dr. David E. Mann, Jr. (Co-investigator)	10	—
Dr. Robert L. Pollack (Co-investigator)	10	—
Technicall		
Biochemist (to be recruited)	100	7,500
Fringe benefits @12.5%		2,438
Sub-Total for A		21,938

B. Consumable supplies (by major categories)	
Chemicals and Glassware	725.00
Chromatographic supplies-resins, plates etc.	625.00
Experimental animals including maintenance	750.00
Spare parts and replacements for SPF	650.00
Duct collection devices	125.00
Sub-Total for B	2,875

C. Other expenses (itemize)	
Fees for paid volunteers	200.00
Sub-Total for C	200
Running Total of A + B + C	$ 25,013

D. Permanent equipment (itemize)	
1 Aminco-Bowman Model 4-8202 Spectrophotofluorometer complete with Power Supply, Microphotometer and Accessories	4,850.00
1 Aminco-Bowman Model 4-8909XY Recorder	1,500.00
1 Aminco-Bowman Time generation device for above	295.00
Sub-Total for D	6,645
E. Indirect costs (15% of A+B+C)	3,752
Total request	$35,410

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15. Estimated future requirements:

	Salaries	Consumable Suppl.	Other Expenses	Permanent Equip.	Indirect Costs	Total
Year 2	R	$2,785	$200	nil	$3936	$30,175
Year 3	---					

16. Other sources of financial support:
List financial support from all sources, including own institution, for this and related research projects.

CURRENTLY ACTIVE

Title of Project	Source (give grant numbers)	Amount	Inclusive Dates
Neurosecretory Components of Human Saliva	Temple University Grant-in-aid, 405-063-75	1,000.00	1 July/72 through 20 June/73

PENDING OR PLANNED

Title of Project	Source (give grant numbers)	Amount	Inclusive Dates
	none		

It is understood that the investigator and institutional officers in applying for a grant have read and accept the Council's "Statement of Policy Containing Conditions and Terms Under Which Project Grants Are Made."

Principal investigator

Typed Name Victor J. Schenker, Ph.D.

Signature [signature] Date 1/26/73

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Temple Univ. Health Science Center

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TUHSC,
3400 N. Broad St. Phila, Penna. 19140

Responsible officer of institution

Typed Name David W. Siegel

Title Assoc. V. P. for Administration

Signature [signature] Date 1/26/73

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10035388886

1. Research Plan

A. Introduction and Specific Aims

The proposed study represents one facet of this department's total research program in oral biochemistry and physiology. The study is an extension of previous work by the principal investigator which provides presumptive evidence that: 1) human saliva contains material comprising amine-like compounds with neuroactive effects which, in mice, are apparently antagonized by low doses of nicotine; 2) this material is also found in homogenates of submaxillary gland tissues from humans and Rhesus macaque monkeys; and 3) the level of this material in human saliva is apparently mediated by cholinergic activity of the autonomic nervous system. Briefly stated, the relevant experimental data are as follows: Human whole saliva, collected under standardized conditions and extracted by solvent and/or ion-exchange methods specific for phenolic amines, yields material showing the spectrofluorometric characteristics of tyramine-like amines (Figs. 1,2,3). Preliminary separation procedures using thin-layer chromatography with specific dye reagents show the presence of a number of phenolic amine-like constituents some of which show the spectrofluorometric characteristics of tyramine. The pharmacologic action of purified extracts on the aortic spiral strip preparation from rabbits pretreated with iponiazid was the same as that of authentic p-tyramine HCl (3×10^{-5} M) with inhibition by 2×10^{-5} M cocaine. Pilot tests in dogs with heart catheterization showed that small amounts of extract introduced directly into the right heart elicited marked increases in right ventricular pressure and pulmonary circuit. Pretreatment i.v. of mice with small amounts of lyophylized, purified extracts containing microgram amounts of salivary fluorophore (SF) produce a 2- to 3-fold prolongation of hexobarbital induced sleeping time (Table 1) as does a 2μg i.v. dose of authentic p-tyramine HCl. Preliminary tests in mice indicate that such potention by SF does not occur when nicotine alkaloid (0.01 mg/kg) is injected together with the extract. Using quantitative spectrofluorometric procedures to measure salivary SF levels in healthy human subjects, it was found that a single small dose (4 mg in 0.8 ml., s.c.) of the cholinergic agent urecholine elicited a marked increase (up to

6-fold over the saliva control) of SF in saliva within 30 minutes; this increase was not positively correlated with flow volume and subsided to preinjection levels during the subsequent 1-1.5 hours. In contrast, atropine (0.64 mg in 1.6 ml, s.c.) produced the opposite effect; there was a prolonged decrease in SF. Epinephrine (0.3 ml of 10^{-3} adrenaline chloride, s.c.) did not uniformly elicit the marked transitory peak response shown by urecholine; epinephrine showed a prolonged gradual increase in SF parallel to that seen in the saliva control curves, (Figs, 4 and 5).

In an attempt to interpret these combined findings physiologically, an overall working hypothesis has been formulated, thus 1) human saliva contains one or more neuroactive biogenic amines ostensibly elaborated by and/or released from the submaxillary salivary glands under the mediation or modulation of the sutonomic nervous system; and 2) such compounds, continuously present in the oral cavity in varying amounts - depending upon autonomic activity - may be absorbed through the oral mucosa and transported directly to the right heart and, via the pulmonary circuit, reach the brain and other organs before chemical alteration by passage through the hepatic or renal circulation. This vascular shunt could thus facilitate the homeostatic interaction of these compounds with other regulatory factors at extra-oral sites. This working hypothesis constitutes a major basis for the present specific aims as well as our long-range goals.

In this context, the preliminary finding that nicotine is an apparent antagonist to SF is of some interest. It is generally recognized that nicotine is absorbed through the oral mucosa, and its pharmacological actions in the central nervous system have been comprehensively reviewed by Silvette, et al.(1). It is therefore intended, in our studies, to place emphasis upon the interactions between SF and nicotine (both pharmacologic and neurochemical) in the CNS. Not only will this exploit this drug as a tool for the pharmacologic characterization of an ostensibly neuroactive substance, but, at the same time, it will disclose possible new information about nicotine mechanisms in the CNS. This is all the more appropriate in the light of the amine-like character of SF and the reported relationship between this agent and catechol amines which stem from the same amino acid precursors as do those contained in SF. (26,27).

With these considerations in mind, our initial specific aims will be directed primarily at the precise chemical identification of the individual components of SF as demonstrated by our chromatographic separation studies. As indicated above,

pharmacological testing, in collaboration with Professor David E. Mann, Jr., of the Department of Pharmacology, School of Pharmacy, will be done concurrently on whole extracts, and, as they become available, on separate chemical fractions. In addition, correlative neurochemical analyses will be made in animal brain. We therefore hope to establish, on the basis of precise pharmacological characterization, which component(s) is active in producing the pharmacological effects shown by the whole extracts as well as the neurochemical correlates of these effects. With the achievement of these aims, a firm basis will have been established for the further studies necessary to achieve our long-range goals as stated in our overall working hypothesis.

B. Method of Procedure

a) Collection of Saliva Samples. Saliva specimens will be collected under controlled procedures previously established. Donors will comprise healthy adult, male, paid volunteers recruited from the university staff and/or the student body. Samples for analysis will be collected both as whole saliva and as duct saliva drawn differentially by means of duct cap devices as routinely used in this laboratory. All specimens will be collected approximately at the same time of day (mid-morning), over timed intervals, and transferred directly into chilled graduated receptacles containing measured amounts of ethanol so that the final sample will comprise a solution of saliva in 70% ethanol. This procedure serves both to curtail bacterial action and to provide precipitation of protein which, with appropriate addition of acetone and acidification to pH 4.5, is a necessary preparatory step for the subsequent ion-exchange column separation procedure. Collections will be made both with and without stimulation. The latter will be induced, as indicated by the specific experimental conditions, by passive chewing of paraffin for collection of whole saliva, controlled application of lemon juice to the tongue for duct saliva, or a single subcutaneous injection of 3-4 mg of urecholine (Bethanicol chloride, Merck) under appropriate supervision as in previous studies. Complete records will be made of subjects' age, height, weight, smoking habits, general state of health and nutrition as well as gross subjective feelings and affect prior to and during specimen collection. Candidates will be instructed to refrain from smoking for at least 2-3 hours prior to collection, and from the ingestion of

alcohol and all drugs (especially aspirin or psychotropic tranquillizers, etc.) for at least 24 hours prior to specimen collection. Those requiring medication of any kind for any reason will not be accepted.

b) Preparation of SF extracts. The procedure to be used is essentially that of Kakimoto & Armstrong (2) as applied by Boulton (3) for the extraction of phenolic amines from urine, and modified by us for application to saliva. Saliva samples in 70% ethanol at pH 4.5 are centrifuged and filtered to remove precipitated protein, then applied to a column of appropriately pretreated Dowex 50W resin in the H^+ form. Conjugated compounds, neutral and most of the basic aliphatic substances are removed by appropriate washings with water and sodium acetate. The aromatic amines retained on the resin are eluted with N/1 NH_4OH in 65% ethanol and the eluate taken to dryness in vacuo at 40°C. The dried residue is extracted into absolute ethanol and centrifuged to remove any insoluble material. The clear supernate is quantitatively divided into 2 portions, one for quantitative spectrofluorometric examination at maximal activation & fluorescence and for thin-layer chromatographic (TLC) separation, and the other for reconstitution into aqueous solutions for testing in animals.

c) Chemical Separation and Identification of SF Extracts: Extracts prepared as described above will be concentrated to small volume, applied to silica gel thin-layer plates, and developed under standard conditions using the appropriate solvent systems as worked out in our previous studies, to ascertain the R_f properties of various extract components. Information as to chemical structure of individual spots will be sought by the use of various specific color developing agents for comparison with authentic phenylethyl- and phenylethanolamines and their derivatives used as reference standards. Eluted fractions of extracts striped on plates and located in this manner will be rechromatographed singly and in combination with reference compounds and further examined for absorption spectra, spectrofluorometric characteristics, as well as infra red spectroscopic patterns using procedures such as those described by Kirschenbaum and Parker (4).

d) Pharmacological Evaluation: The following pharmacological procedures will be conducted to ascertain the nature of SF whose initial screening characteristics suggest tyramine-like activity in mice:

1. Hexobarbital sleeping time: Because preliminary screening studies have revealed that SF can potentiate hexobarbital sleeping time in mice and also that nicotine on the one hand and tyramine on the other can inhibit and prolong sleeping time respectively, the following experiments will be executed to elucidate the underlying mechanisms involved in sleeping time alteration and to determine whether SF elicits effects comparable to those produced by tyramine under similar conditions.

Treatment regimen:	Measurement of:
low doses of nicotine + SF + hexobarbital)	duration of sleep
low saline control " ")	
high doses of nicotine + SF + hexobarbital)	" " "
high saline control " ")	
low dose(nicotine) + tyramine + hexobarbital)	" " "
low saline control " ")	
high dose(nicotine) + tyramine + hexobarbital)	" " "
high saline control)	

If tyramine and SF responses are similar in the presence of low or high doses of nicotine with respect to alterations in sleeping time, then confirmation of tyramine-like activity is made with respect to its relationship in the presence of a ganglionic blocking agent. If sleeping time is shortened in the presence of nicotine and SF as compared to saline and SF, the recognition of central neural sites for the action of SF will be indicated. However, nicotine stimulates then causes ganglionic depression; therefore, it is necessary to administer a pure (depressant only) gangliolytic agent in place of nicotine to determine that ganglionic depression instead of stimulation is responsible for the inhibition of the central effects induced by SF in the presence of hexobarbital. Thus:

	Measurement of:
Hexamethonium chloride + tyramine + hexobarbital)	duration s.t.
saline control " ")	
Hexamethonium chloride + SF + hexobarbital)	" "
saline control)	

If sleeping time is shortened significantly when either tyramine or SF is administered in the presence of C_6, this will indicate that ganglionic depression centrally is responsible for the inhibition of tyramine or SF potentiation of hexobarbital sleeping time rather than initial stimulation caused

by nicotine in the earlier experiment.

2. Isolated Mercenaria mercenaria heart studies: Previous studies utilizing the isolated heart of Mercenaria mercenaria suspended in sea water and attached to a recording device have revealed that successive administrations of norepinephrine rapidly cause the development of tachyphylaxis characterized by first a negative inotropic response that shortly disappears by the third or fourth administration (5). This procedure affords an excellent means by which the pharmacological similarities of tyramine and SF can be compared or contrasted.

PROCEDURES: The isolated heart is suspended in a 40 ml. chamber containing sea water at room temperature (24-30°) and aerated with air. Successive administrations of either tyramine at constant dosage levels or SF will be made at intervals governed by the time required for normalcy of contractions to return. In addition, the prior administration of tyramine followed by known tachyphylactic doses of norepinephrine (NE) and SF followed by NE will be studied to ascertain whether deviations in NE-induced tachyphylaxis occur.

3. Influence of SF and Tyramine on Sodium Nitro-Prusside and Hypothermia in Mature Mice: We have recently demonstrated in our laboratory that oxotremorine and sodium nitroprusside each produce hypothermia in mature mice via a different mechanism (6). The parasympathomimetic, pilocarpine, did not alter oxotremorine-induced hypothermia, but partially inhibited that produced by sodium nitroprusside. Conversely, atropine inhibited oxotremorine-induced hypothermia, but failed to modify that elicited by sodium nitroprusside.

PROCEDURE: Mature mice will be divided into groups and treated as follows:

Rectal temperatures recorded immediately prior to start of treatment. 1-SF injection s.c., 15 minutes later rectal temperature recorded, oxotremorine admin. i.p., 15 minutes later, final rectal temp. recording; 2-tyramine injected, s.c., 15 minutes later rectal temperature recorded, oxotremorine admin., i.p., then

15 minutes later, final rectal temp. recorded. The procedure is repeated using sodium nitroprusside in place of oxotremorine.

The influence of tyramine on either sodium nitroprusside-or oxotremorine-induced hypothermia has not been studied by us. Therefore, if comparable results are obtained with each hypothermic agent, following the injection of SF or tyramine, further proof of their close pharmacological characters will accrue.

4. Influence of SF and Tyramine on Nicotine Convulsions and Tremor in Young Mice.

The central action of nicotine in eliciting both convulsions and tremor is well known, and has found use in the evaluation of anti-convulsive as well as anti-tremor properties of many pharmaceutical preparations. This approach will be applied to testing SF and tyramine for relative anti-nicotine action. Methods of procedure using mice have been reported by a number of authors (7-11). These methods will be applied as follows:

PROCEDURE: Mice (18-26 gm) will be divided into groups and treated as follows:

1. Nicotine at low doses intracerebrally...observe tremor
   SF + nicotine " " " ... " "
   Saline controls..... " effects of i/c injection

2. As in 1 above but using tyramine instead of SF..observe tremor
3. Nicotine at convulsive doses i/c .....observe convulsions
   SF + nicotine " " " ..... "
   "
   Saline control..... "
   "
4. Ditto using tyramine instead of SF.....observe convulsions

e) Neurochemical Studies: The following procedures are intended to provide some neurochemical parameters of the pharmacological data from the previous section, and at the same time, to furnish some points of departure for future more detailed studies. Biochemical observations will be confined to the

measurement of norepinephrine (NE), dopamine (DPA) and serotonin (5HT) in extracts of whole brain homogenates of mice according to the method of Snyder, Axelrod and Zweig (18) as modified by Welsh & Welsh (12) and Leonard & Shallice (13). These estimations will be made in groups of mice injected according to the respective treatment schedules used for the pharmacological evaluation procedures. Because hexobarbital sleeping-time potentiation has been related to the brain amine-depletion effects of reserpine, uptake and release mechanisms become important neurochemical considerations with respect to our study of SF and its 'antagonist', nicotine. Accordingly, the above experiments will be extended to include observations on the effects, on the three brain amines mentioned, of SF, p-tyramine and derivatives, and nicotine. For this purpose, the experimental preparation will comprise mice pre-treated with reserpine, and in addition, with 4-α-dimethyl-m-tyramine (H77/77), a compound which has been found to displace brain catechol amines - particularly NE - and utilizes the reserpine-resistant uptake mechanisms to effect this displacement (19,20,21). This approach has been utilized recently by Leonard & Shallice (13) for studying the effects of phenylethylamines in brain and provides a suitable procedure for our comparative studies of SF, p-tyramine and nicotine.

C. Significance of this Research

This work concerns primarily a study of the relationship between autonomic nervous system activity and the biogenic amines in their role(s) as neurohumoral agents. Apart from the academic significance of our original discovery indicating the presence of such compounds in human saliva (15), the quantitative changes in their concentration after cholinergic stimulation immediately suggests a possible compensatory release of adrenergic amines in response to a cholinergic stimulus. In addition, such consideration would indicate a means of measuring, in humans, comparative autonomic responsivity to controlled cholinergic challenge by low doses of accepted pharmacological agents (see attached reprint of ref. 15 illustrating the marked differences between healthy controls and patients with severe alcoholism in their responses to urecholine challenge). In other words, these findings, substantiated as to interpretation by the proposed extended studies, could provide a relatively simple approach to the biochemical evaluation of an important aspect of autonomic status in terms of changes in the biogenic amines, which in themselves play an important part in the regulation of activity within the nervous system. The presence of SF in

the submaxillary gland as well as in the saliva could be expected to reflect cellular activity in a gland which in turn, develops embryologically from the same oropharyngeal mucosa as does the anterior hypophysis. In this context, the salivary gland and its secretory products would appear to be an organ of choice for studying the neurochemical correlates of autonomic function in man. Further significance would stem from the application of these extended studies to the elucidation of the central actions of nicotine. In addition to the direct evidence stemming from our neurochemical studies of nicotine in animal brain, useful information on the autonomic effects of this drug - absorbed from the oral mucosa - could be obtained from tests in humans smoking tobacco under controlled conditions. The significance of the concept involving the oral absorption of neuroactive salivary components to fulfill homeostatic interactive functions at extra-oral sites, as stated in our overall working hypothesis, is that it presents a hitherto unrecognized role of the salivary glands as participants in regulatory neural mechanisms - an important new facet of oral biology. A fuller significance of these various aspects is expected to emerge from the extended research of this proposal.

D. Space and Facilities Available

The Biochemistry Department at the Temple University School of Dentistry has some 2,000 sq. ft. of newly renovated research space available in two large rooms with the use of a working cold room, fume hoods, and vented space for various types of chromatography, as well as offices and secretarial assistance.

The equipment available in the department includes: one Spinco RC-2B refrigerated ultra-centrifuge, two rotors (SW-25.1 and a 65), two Servall refrigerated centrifuges (one RC-2 and one SE-1), two size 2 ICI centrifuges kept in a cold room, and various table top centrifuges.

There are two Gilford 2000 recording spectrophotometers, one Perkin-Elmer Hitachi spectrophotometer, one Spectronic 505 spectrophotometer, one Spectronic 20, and two Coleman Junior visible spectrophotometers. There is also an Aminco-Rosett Recording Fluorimeter, and an Evans Atomic Absorption spectrophotometer.

There are three fraction collectors, three expanded scale pH meters, various microscopes, one Frieden bench top computer and a Lago-marsino calculator, gel and strip electrophoresis equipment, thin-layer and paper chromatograph, three 18-station Warburg respirometers, one of which is refrigerated, two recording oxygen electrodes and a Radiometer carbon dioxide monitor, various micro-, semimicro- and macro balances, three mini-pumps and various columns for column chromatography, two lyophilizers, and a gradient former and eluter for the ultra-centrifuge.

Available for our use within the Dental School are electron microscope service, histology service, a complete department for photography, art, and illustration, extensive animal care facilities, a complete radioisotope laboratory, a nuclear magnetic resonance service, and the advice and assistance of the staff of a large, well-functioning dental school. Pharmacological facilities are available within the School of Pharmacy.

The Aminco-Bowman Spectrophotofluorometer and Recorder are the only additional pieces of permanent equipment required for this work. The instrument presently available to us is on temporary loan. A new instrument is consequently being requested under the present budget.

2. Supporting Data

A. Previous Work by the Investigator Related to This Project

Our previous findings of immediate relevance to the present studies have been outlined in the previous Section 1-A. Details appear in reference No.'s 15-17 below, and in appended figures. Other relevant studies include experiments in rats - extending those of Schneyer & Schneyer (22,23) - which indicated significant increases in submaxillary gland amylase activity concomitant with immobilization stress without physical injury per se, but with resultant severe gastrointestinal ulceration. These unpublished experiments (25) illustrate further the chemical alterations in the salivary gland concomitant with augmented autonomic activity, whether induced by pharmacological agents (22) or by the psychological stress of immobilization.

B. Pertinent Literature References

Our original finding of SF in human whole saliva has been confirmed by Hamby, et al.(24). Neuroactive substances in saliva and salivary glands of animals have been widely recognized for many years. Among those relevant to our studies are the early reports of Cattell, et al.(28) describing a neurohumoral agent with the properties of "adrenin" from cat submaxillary glands. The classical studies of Babkin and his associates (29) include extensive reports on various vasoactive substances (other than bradykinin or kallicrein) which vary in activity with autonomic stimulation. Similar findings have been reported by Hilton & Lewis (30). Stromblad (31,32) has described a monoamine oxidase acting upon tyramine substrate in the submaxillary glands of humans and animals. Most of the studies in human salivary gland function relative to the ANS have been restricted to salivary flow rate, and to some extent, electrolyte changes, although Giddon & Lisanti (33) have reported the occurrence of a cholinesterase-like substance in the parotid saliva of 'normal' and psychiatric patients. Of interest relative to biogenic amines is the report of Selye, et al. (34) demonstrating a five-fold increase in size of rats' submaxillary glands following chronic treatment with isoproterenol. This growth-stimulating action is reminiscent of the nerve-growth factor (NGF) effect upon sympathetic nerve tissue by extracts of mouse submaxillary glands reported by Levi-Montalcini & Cohen (35). Evidence relating to extra-oral sites of action of submaxillary gland products is seen in various accounts of the ostensible "hormone activity" of submaxillary gland tissue implants in the sella of the hypophysectomized dog by Alvarez-Buylla (37) in which the effects of hypophysectomy were almost entirely reversed in the presence of the implanted salivary gland. Evidence for a non-exocrine function of the submaxillary gland is presented in the growth experiments of Narasimhan & Ganla (36) in mice, rats, dogs and monkeys, and Godlowski & Calandra (39,40) have described an "insulin inhibitor" factor from dog submaxillary glands, thus suggesting an endocrine function for these gland structures. Our concept of the possible absorption of SF into the blood stream through the oral mucosa receives support from the recognized use of the sublingual route of administration of a variety of compounds including various steroid hormones in endocrinopathies, nitroglycerine in cardiac disorders, and isoproterenol in asthma. A direct pathway from the oral cavity to the brain has been described by Kare (38).

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(with L.S. Maynard)

MONOAMINE OXIDASE INHIBITION BY ETHANOL IN VITRO.
Nature, 196:575, 1962.
(with L.S. Maynard)

A BIOCHEMICAL CORRELATE OF AUTONOMIC ACTIVITY: THE EFFECT OF BETHANECHOL ON SERUM AMYLASE IN DOGS.
Surgery, 56:394, 1964.
(with R.M. Engelman, P. Polimeni, M. Stucker, A. Riddick, A.C. Schenker and J.H. Stuckey)

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Psychosom. Med., XXVIII, No. 4: Part II 564-569, 1966.
(with A.C. Schenker, D. Kissin & L.S. Maynard)

THE EFFECTS OF ETHANOL ON AMINE METABOLISM IN ALCOHOLISM.
In: Biochemical Factors in Alcoholism, pp. 39-52, R.P. Maickel (ed.), Pergamon Press, Oxford & New York, 1966.
(with B. Kissin, L.S. Maynard & A.C. Schenker)

EFFECTS OF ETHANOL ON THE ENDOCRINES.
In: Internat'l Encyclopedia of Pharmacology and Therapeutics, Section 20, Vol. 1, Chap. 10, J. Tromolieres (ed.), Pergamon Press, 1970.

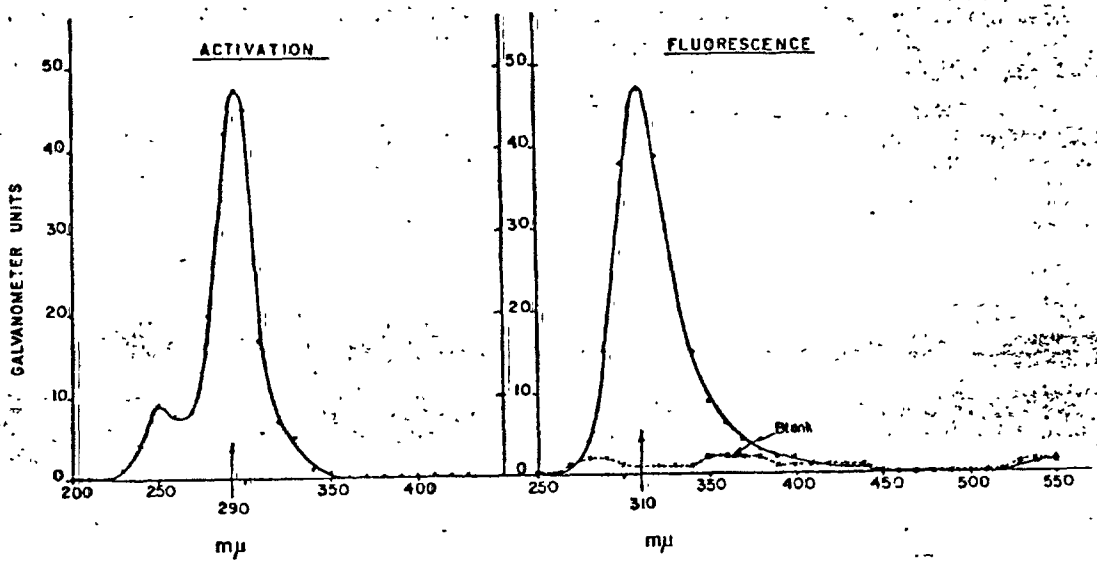

Figure 1. Activation and fluorescence spectra of the salivary factor (SF) extracted from human mixed saliva. Extracts of homogenized human submaxillary glands show identical spectra. Maximum fluorescence: 310 mμ, maximum activation 275 mμ (290 mμ corrected).

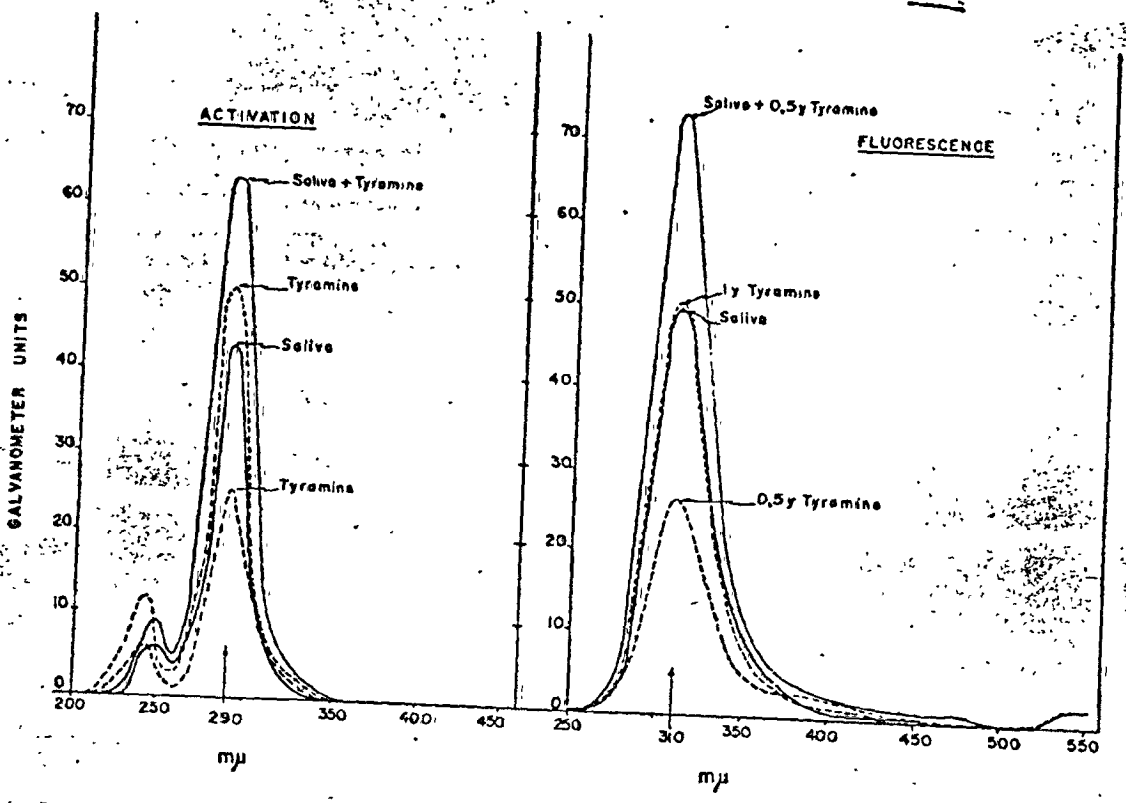

Figure 2. Comparative maximal activation and fluorescence curves of p-tyramine, and whole saliva with and without added p-tyramine all identically extracted. Note similarity between the salivary factor (SF) and authentic p-tyramine with activation at 290 mμ (corrected = 275 mμ) and fluorescence at 310 mμ.

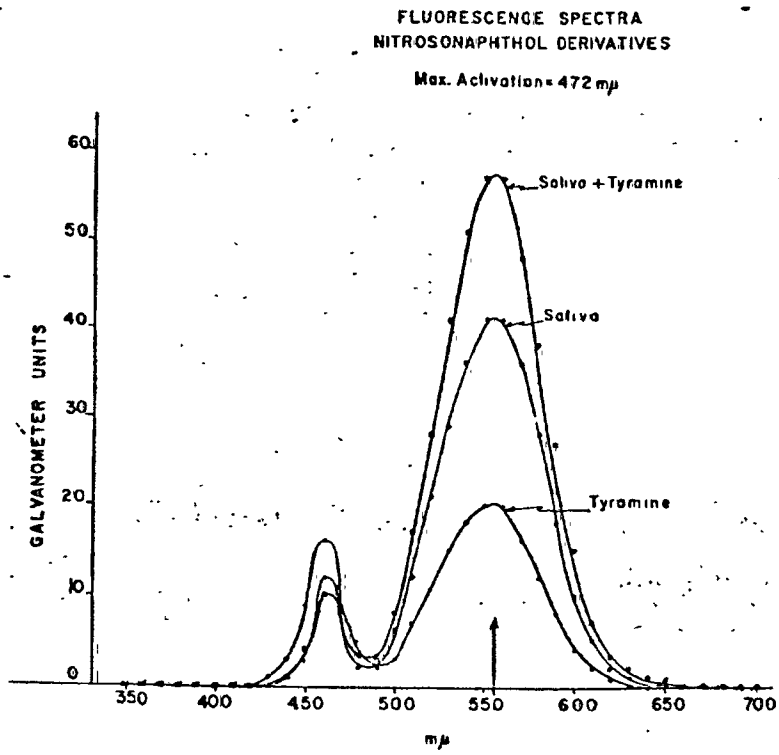

Figure 3. Fluorescence spectra of nitrosonaphthol-HNO_3 derivatives of p-tyramine and human whole saliva extracts, singly and in combination. Maximum fluorescence: 550-560 mμ, maximum activation 472 mμ. Note correspondance of curves for these derivatives.

TABLE I

EFFECT OF SALIVA EXTRACT ON HEXOBARBITONE HYPNOSIS

Minutes Sleeping Time*	
Blank Extract † plus Hexobarbitone	Saliva Extract § plus Hexobarbitone
20.3 ± 8.5 (10)	46.8 ± 6.8 (10)

* Interval between Loss & Recovery of Righting Reflex
† Water Blank carried through entire extraction procedure
§ 0.4 ml Extract, i/v, 17 minutes before evipal (100mg/Kg) i/p.

Table 1. The effects pre-treatment with extracts containing SF upon the central action of hexobarbitone. Note the greater than 2-fold increase in sleeping time of treated animals over their controls.

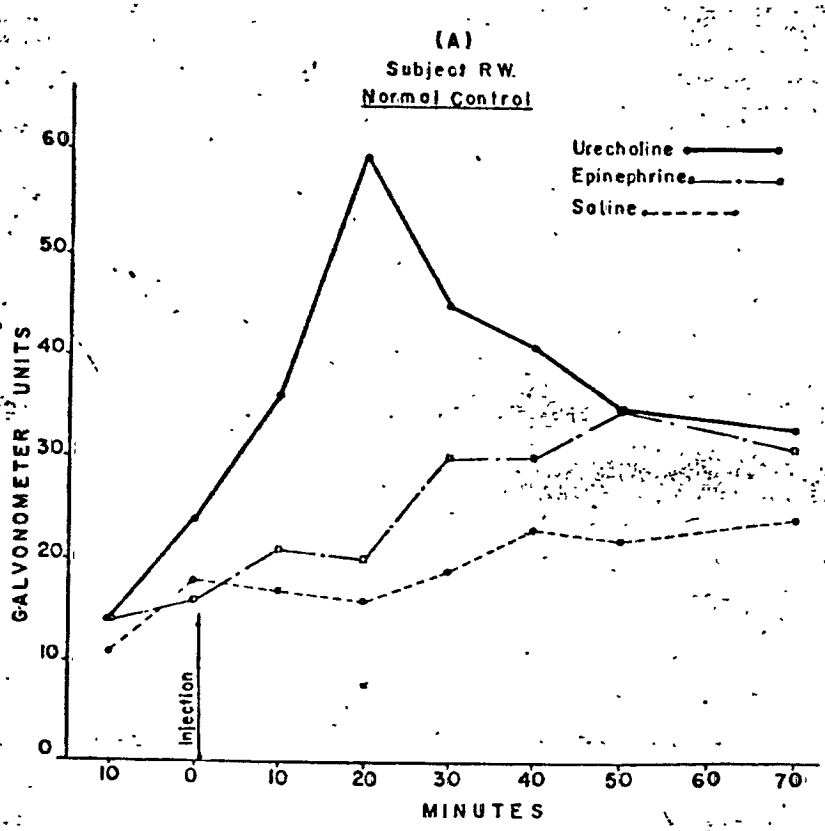

Figure 4. Representative response patterns of changes in SF secretion rate in a healthy male subject following the injection of 4 mg. urecholine (Bethanechol Chloride, Merck); 0.3 ml of 10^{-3} epinephrine (Adrenaline Chloride, Parke Davis); and physiological Saline as control. Note marked response curve after urecholine.

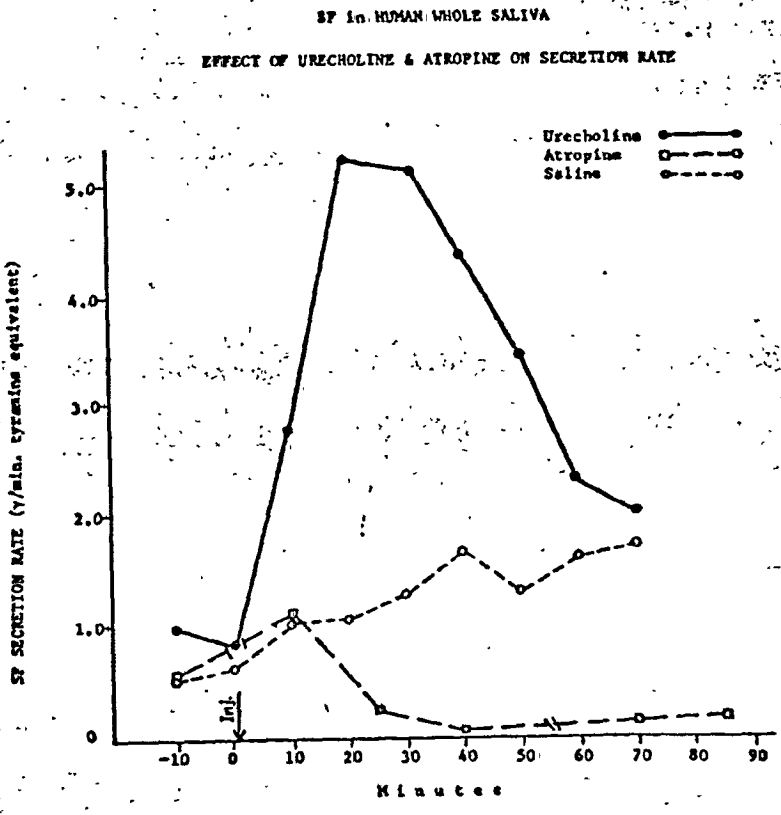

Figure 5. Changes in SF secretion rate in response to injections of urecholine 4 mg., atropine 0.64 mg, and saline control in a healthy adult male subject. Note the opposite effects of atropine and urecholine.

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EDUCATION:

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St. Michael's Academy, Montreal, Canada
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Ecole Technique de Montreal - (Dipl. Tel. Comm'n.; First Award Final Year Thesis: Silver Medal for Second Highest Aggregate Standing.)
McGill University - B.Sc. Degree
McGill University - Ph.D. Degree (cum laude) in Experimental Medicine.

POSITIONS HELD:

1927 - 1932: Out-Plant Engineering, Bell Tel. Co. of Canada. Estimating Engineer, Northern Elec. Co., Montreal, Canada.

1933: Asst. Statistician (part-time) Dept. Social Research, McGill University.

1934 - 1935: Laboratory Technician, Dept. Exp'l Medicine, McGill University, Asst. to Dr. J.J. Day in the laboratories of Prof. B.P. Babkin - Gastroenterological research studies in dogs.

1937 - 1938: Research Assistant, Dept. Anatomy, McGill University - Research Studies on Adrenocortical Aspects of the "Alarm Reaction" under the direction of Dr. Hans Selye. Research Asst., Biol. Labs.; Ayerst, McKenna and Harrison, Ltd., Montreal, Canada, under direction of Dr. A. Stanley Cook.

1939 - 1940: Research Asst., Dept. of Anatomy, McGill University - Studies of effects of the "Alarm Reaction" on Basal Metabolic Rate in Animals - under direction of Dr. Hans Selye.

1940 - 1941: Resumed former position as Research Asst. at Ayerst, McKenna & Harrison Laboratories.

1945 - 1948: Research Associate, Dept. Medicine, McGill University. Later, Research Fellow, McGill Univ. Clinic, Royal Victoria Hospital. Studies on Metabolic and Nutritional Aspects in Patients after Trauma and Drug Convalescence - Under direction of Prof. J.C. Meakins and Dr. J.S.L. Brown

1947: Lecturer, Dept. of Medicine, McGill Univ. Research Fellow, University Clinic, Royal Victoria Hospital - Head, Nutrition Research Laboratory and Member of Attending Staff, Dept. Medicine, Royal Victoria Hospital.

1948 - 1951: Assistant Professor of Medicine, McGill Univ. (ibid)

1951 - 1953: Staff Member, Worcester Foundation for Experimental Biology, Shrewsbury, Mass. (Studies on adrenocortical function in schizophrenia and on biogenesis of adrenocortical hormones, with Drs. G. Pincus, O. Hochtor, and H. Hoagland.

1953 - 1957: Assistant Professor Psychiatry (Biochemistry), State University of N.Y., College of Medicine, Brooklyn, N.Y.

1958 - 1965: Associate Professor of Psychiatry - Director, Biochemical Research Laboratory, State Univ. of N.Y., College of Med.

1965 - 1968: Associate Professor of Biochemistry, Albany College of Medicine, Union Univ. - Chief, Biochemistry, Psychiatry & Aging Research Laboratories, Veterans Administration Hospital, Albany, N.Y.

1968 - 1970: Research Biochemist, Affective Disease Research Unit, Veterans Administration Hospital, Philadelphia, Pa.

1972 - Research Professor of Biochemistry, Dept. of Biochemistry, Temple University School of Dentistry Philadelphia, Pa.

RESUMÉ OF AREAS OF RESEARCH

BIOCHEMICAL & ENDOCRINE FACTORS IN ALCOHOLISM

Adrenal Hormones & Amino Metabolism in Chronic Alcoholics.
Effects of Ethanol on Amine Metabolism in Alcoholism.
Effects of Ethanol on the Endocrines.
(Publ. #53, 54, 58)

Monoamine Oxidase, in vitro Inhibition (Publ. #46)
Decarboxylase Activity in vivo (misc) (" #45)
Pulmonary Respiration Pattern: Effects of Ethanol and Chlorpromazine in Chronic Alcoholics. (Publ. #40, 44)
Acute Effects of Ethanol on Adrenocortical Function, Liver Disease, & Other Physiological Functions in Alcoholic Patients. (Publ. #36, 37, 38)

BIOCHEMICAL & PSYCHOLOGICAL STUDIES (Biochem. Psychopharmacol.)

Monoamine oxidase Inhibition & Antidepressive Correlates in Psychiatric Patients. (Publ. #39)
Biochemical Correlates of Autonomic Function: Salivary Factor; Response to autonomic activity in humans.
(Publ. #35, 51, 43)

ADRENOCORTICAL HORMONES

New Methods of Bioassay in rats. (Publ. #1, 30)
The nature & biogenesis of adrenocorticoids; adrenal perfusion studies. (Publ. #26, 27, 28, 29, 31, 32, 33)
Studies in rats on the effects of the "Alarm Reaction" on basal metabolic rates. (Publ. #2, 3)

METABOLIC ASPECTS OF CONVALESCENCE & WOUND HEALING

Protein Metabolism, Nitrogen Balance, Nutrition, & Adrenocortical Function in patients with disease & after acute injuries. (Publ. #5 thru#24)
(Ph.D. Thesis)

MEMBERSHIPS:

REDACTED

PUBLICATIONS

VICTOR J. SCHENKER

1. A NEW & RAPID METHOD FOR THE ASSAY OF THE HORMONE OF THE ADRENAL CORTEX.
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3. FORMATION OF IRON-PIGMENT LYMPH NODES IN THE RAT.
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4. SOME EFFECTS OF DICOUMARIN - "HAEMORRHAGIC FACTOR" _ IN VIVO & IN VITRO STUDIES.
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7. EFFECTS OF ALTERATIONS IN NITROGEN & CALORIC INTAKE ON THE RATE OF NITROGEN METABOLISM & URINARY 17-KETOSTEROIDS EXCRETION IN PATIENTS & IN HEALTHY SUBJECTS.
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10. SOME METABOLIC ASPECTS OF DAMAGE & CONVALESCENCE.
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11. CHANGES IN NITROGEN METABOLISM AFTER DAMAGE.
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17. STUDIES IN THE HOURLY RATE OF NITROGEN EXCRETION IN PATIENTS AFTER ACUTE INJURY & IN HEALTHY CONTROL SUBJECTS.
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Assoc. Comm. on Army Med. Res., Proc., 10th Meeting, 1947.
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21. CERTAIN ASPECTS OF PROTEIN METABOLISM & NUTRITION IN PATIENTS WITH CHRONIC ILLNESS.
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22. HIGH PROTEIN DIETS.
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(with L.G. Johnson & H.A. Sutherland)

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30. A METHOD OF BIO-ASSAY FOR ADRENOCORTICAL POTENCY BY MEANS OF EXPERIMENTAL TRAUMA WITH SHOCK IN RATS.
Endocrinology, 53:345, 1953.

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1. Mann, David E., Jr., "Effect of orally administered potassium iodate on blood sugar response to thiourea," Proceedings of the Society for Experimental Biology and Medicine, 73, 657-658 (1950);

2. Zarrow, M.X., Denison, M.E., Rosenberg, B., and Mann, D.E., Jr., Neher, G.M., "Effect of insulin and epinephrine on the eosinophil and blood glucose levels in sheep; lack of diurnal rhythm," The American Journal of Physiology, 171, 636-640(1952);

3. McCreesh, A. H., and Mann, David E., Jr., "The effect of orally administered sodium iodide and sodium iodate on blood sugar response to thiourea in the rat," Journal of American Pharmaceutical Association, scientific edition, 47, 56-57 (1958);

4. Fujita, T., and Mann, David E., Jr., "Further studies on l-arterenol tachyphylaxis in the isolated heart of Venus mercenaria," Journal of the American Pharmaceutical Association, scientific edition, 47, 90-93 (1958);

5. Gautieri, R.F., and Mann, David E., Jr., "Determination of the minimal carcinogenic $dose_{50}$ of methylcholanthrene on mouse epidermis," Journal of the American Pharmaceutical Association, scientific edition, 47, 350-353 (1958);

6. Goldenberg, M.M., and Mann, David E., Jr., "The antidotal effectiveness of sodium cobaltinitrite in antagonizing cyanide poisoning in albino mice," Journal of the American Pharmaceutical Association, scientific edition, 49, 210-212 (1960);

7. Gautieri, R.F., and Mann, David E., Jr., "Effect of gonadectomy and estradiol benzoate administration on the minimal carcinogenic $dose_{50}$ of methylcholanthrene on mouse epidermis," Journal of Pharmaceutical Sciences, 50, 556-560 (1961);

8. Ciuchta, H. P., and Mann, David E., Jr., "Effects of dl-, l-, and d-ephedrine on levarterenol tachyphylaxis in the isolated heart of Venus mercenaria," Journal of Pharmaceutical Sciences, 50, 648-651 (1961);

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9. Bagdon, W.J., and Mann, David E., Jr., "Chlorpromazine hyperthermia in young albino mice," Journal of Pharmaceutical Sciences, 51, 753-755 (1962);

10. Orzechowski, R.F., and Mann, David E., Jr., "Effects of dl-, d-, and l-amphetamine on levarterenol tachyphylaxis in the isolated heart of Venus mercenaria," Journal of Pharmaceutical Sciences, 52, 337-340 (1963);

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12. Orzechowski, R.F., Gautieri, R.F., and Mann, David E., Jr., "Effect of sodium nitrite and p-aminopropiophenone on the minimal carcinogenic dose$_{50}$ of methylcholanthrene on mouse epidermis, " Journal of Pharmaceutical Sciences, 54, 64-66 (1965);

13. Orzechowski, R.F., Gautieri, R.F., and Mann, David E., Jr., "Effect of sodium cobaltinitrite on the minimal carcinogenic dose$_{50}$ of methylcholanthrene in albino mice," Journal of Pharmaceutical Sciences, 53, 388-391 (1964);

14. Harpel, Howard S., Jr., and Mann, David E., Jr., "Antagonism of dextro-propoxyphene poisoning in albino mice with nalorphine HCl, levallorphan tartrate, and methylene blue," Journal of Pharmaceutical Sciences, 54, 97-100 (1965);

15. Bagdon, W.J., and Mann, David E., Jr., "Promazine hyperthermia in young albino mice," Journal of Pharmaceutical Sciences, 54, 153-154 (1965);

16. Bagdon, W.J., and Mann, David E., Jr., "Factors modifying chlorpromazine hyperthermia in young albino mice, " Journal of Pharmaceutical Sciences, 54, 240-246(1965);

17. Thompson, R.S., Gautieri, R.F., and Mann, David E., Jr., "Effect of chronic oral administration of sodium cobaltinitrite and sodium nitrite on the minimal carcinogenic dose$_{50}$ of methylcholanthrene in albino mice, " Journal of Pharmaceutical Sciences, 54, 595-598 (1965);

18. Kasirsky, G., Gautieri, R.F., and Mann, David E., Jr., "Effect of cobaltous chloride on the minimal carcinogenic dose$_{50}$ of methylcholanthrene in albino mice, " Journal of Pharmaceutical Sciences, 54, 491-493 (1965);

19. Mann, David E., Jr., "Antagonism of propoxyphene poisoning in albino mice with nalorphine HCl, methylene blue, and tolonium chloride, " Journal of Pharmaceutical Sciences, 56, 130-131 (1967);

31. CHEMICAL TRANSFORMATIONS OF STEROIDS BY ADRENAL PERFUSION, I: PERFUSION METHODS.
Endocrinology, 52:679, 1953.
(with H. Levy, R. Jeanloz, C.W. Marshall, R.P. Jacobsen, O. Hechter, & G. Pincus)

32. CHEMICAL TRANSFORMATIONS OF STEROIDS BY ADRENAL PERFUSION, II: 11-DESOXYCORTICOSTERONE & 17-HYDROXY, 11-DESOXYCORTICOSTERONE.
Jour. Biol. Chem., 203:4333, 1953.
(with H. Levy, R. Jeanloz, C.W. Marshall, R.P. Jacobsen, O. Hechter, & G. Pincus)

33. CHEMICAL TRANSFORMATIONS OF STEROIDS BY ADRENAL PERFUSION.
Jour. Biol. Chem., 211, 2:867, 1954.
(with H. Levy, R. Jeanloz, R.P. Jacobsen, O. Hechter, & G. Pincus)

34. SERIAL LIVER FUNCTION AND BLOOD STUDIES IN PATIENTS RECEIVING CHLORPROMAZINE.
New Eng. Jour. Med. 256:1, 1957.
(with R. Dickes & L. Deutsch)

35. STUDIES ON HUMAN SALIVA: A TYRAMINE-LIKE COMPONENT AND ITS RESPONSE TO AUTONOMIC STIMULATION.
Jour. Nerv. & Ment. Dis., 128(6):520, 1959.
(with Anne C. Schenker)

36. THE ACUTE EFFECTS OF ETHYL ALCOHOL & CHLORPROMAZINE ON CERTAIN PHYSIOLOGICAL FUNCTIONS IN ALCOHOLICS.
Quart. Jour. Studies Alcohol, 20:480, 1959.
(with B. Kissin & A.C. Schenker)

37. ADRENAL CORTICAL FUNCTION AND LIVER DISEASE IN CHRONIC ALCOHOLICS.
Am. Jour. Med. Sci., 238:344, 1959.
(with B. Kisson & A.C. Schenker)

38. THE ACUTE EFFECT OF ETHANOL INGESTION ON PLASMA & URINARY 17-HYDROXYCORTICOIDS IN ALCOHOLIC SUBJECTS.
Am. Jour. Med. Sci., 239:690, 1960.
(with B. Kissin & A.C. Schenker)

39. MONOAMINE OXIDASE INHIBITION AND ANTIDEPRESSIVE CORRELATES.
Proc. Third World Congress Psychiatry, Vol. I, pp. 642-649, 1961.
(with G. Marjerrison, P. Schlachet, N. Freedman, L.D. Hankoff, and D.M. Engelhardt)

40. ABERRATIONS IN THE PULMONARY RESPIRATORY PATTERN IN ALCOHOLICS & THE ACUTE EFFECTS OF ETHYL ALCOHOL & CHLORPROMAZINE UPON SUCH PATTERNS.

Ibid., Vol. I, pp. 389-396, 1961.
(with A.C. Schenker & B. Kissin)

41. CEREBROSPINAL FLUID CATION LEVELS IN DELERIUM TREMENS WITH SPECIAL REFERENCE TO MAGNESIUM.

Jour. Nerv. Ment. Dis., 134;410, 1962.
(with L.S. Glickman, S. Grolnick, A. Green, & A.C. Schenker)

42. EFFECTS OF ETHANOL ON MONOAMINE OXIDASE, PRELIM. STUDIES IN HUMANS & MOUSE TISSUES.
Proc. of Symposium on Biochem. Factors in Alcoholism, N.Y. Acad. Med. Dec. 1961.
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51. AN APPARENT "PRIMATE SPECIFIC" SALIVARY AMINE.
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52. EFFECTS OF STRESS ON TISSUE UPTAKE OF BIOGENIC AMINES: THE MODIFYING INFLUENCE OF MORPHINE SULFATE & OF ALCOHOL.
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54. THE EFFECTS OF ETHANOL ON AMINE METABOLISM IN ALCOHOLISM.
In: Biochemical Factors in Alcoholism, pp. 39-52, R.P. Maickel (Ed) Pergamon Press, Oxford & New York, 1966.
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55. INDUCED HEMORRHAGIC HYPOTENSION: ITS EFFECT ON PLASMA 5-HYDROXYTRYPTAMINE AND PLASMA 5-HYDROXYINDOLE ACETIC ACID LEVELS.
Arch. Surg., 98:194-198, 1969.
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56. PLASMA SEROTONIN LEVELS IN STORED HUMAN BLOOD.
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57. URINARY EXCRETION OF EPINEPHRINE, NOREPINEPHRINE, DOPAMINE AND TRYPTAMINE DURING SLEEP AND WAKEFULNESS.
In: Psychopharmacologia (Berl.) 14:359-370 (1969)
(with Fredrick Baekland, Anne C. Schenker & Richard Lasky)

58. EFFECTS OF ETHANOL ON THE ENDOCRINES.
In: INternat'l Encyclopedia of Pharmacology and Therapeutics, Section 20, Vol. 1, Chap. 10, J. Tromolieres (Ed) Pergamon Press, 1970.

FACULTY VITAE - DAVID E. MANN, JR.

BORN: Johnson City Tennessee, R

Education: Needham High School. R
Harvard College, R , B.S.
Tufts College and Medical School, R
U.S.N.R., R
Boston University, R
Purdue University, M.S. (physiology); R
Purdue University, Ph.D. (physiology);

Employment: Laboratory technician, Boston Consolidated Gas Co., 1947
Assistant professor of physiology and pharmacology, Temple University School of Pharmacy, 1950
Instructor in physiology, Purdue University (summer school), 1951
Associate professor of pharmacology; dept. chairman, Schools of pharmacy and dentistry of Temple University, 1954
Professor of pharmacology, 1960

Society Membership:

REDACTED

Honors and Awards:

Lindback Award for Teaching, June, 1966
Certificate of Merit, Dictionary of International Biography, July, 1967
Inclusion in 1970 edition of "Outstanding Educators of America"
President of the Temple Chapter of Sigma Xi, 1960-61

Biographical references:

Who's Who in the East
The Blue Book
Dictionary of International Biography
Two Thousand Men of Achievement
American Men and Women of Science

Faculty Vitae - David E. Mann, Jr. (Continued)

GRANTS AWARDED:

Title	Grantor Institution	Date Awarded	Amount
1. "Effect of tobacco smoke and residues on methylcholanthrene-induced skin carcinogenesis"	Tobacco Industry Research Committee	9/24/54	5,500.00
Renewal		9/20/55	1,988.00
2. "Factors in development of l-arterenol tachyphylaxis"	N I H	10/5/59	3,335.00
Renewal		10/1/60	3,335.00
3. "Methemoglobinemia and carcinogenesis"	N I H	1/1/62	15,850.00
Renewal		1/7/63	10,898.00
4. "Factors modifying chlorpromazine hyperthermia"	N I H	6/27/63	3,383.00
5. "Effect of vasodilators on perfused human placenta"	N I H	5/1/62	8,395.00
Renewal		5/1/63	8,346.00
Renewal		5/1/64	4,345.00
6. "Chronic methemoglobinemia and carcinogenesis"	Damon Runyon	6/1/63	5,500.00
7. "Modification of Teratogenicity by cobalt"	N I H	5/1/66	12,475.00
Renewal		5/1/67	12,475.00

INVENTIONS:

Two patents (one design patent)
Invented ejector seat used in James Bond film, "Goldfinger;" Popular Science, February, 1947 (page 110) and Popular Science, March, 1966 (page 13).

Publications

Laboratory Manual:

"A Laboratory Manual of Pharmacology," by David E. Mann, Jr. First printed in 1954 and since then used at Temple University in the school of pharmacy and also at the pharmacy schools of the following universities: Montana, Texas, and excerpts at P.C.P.&S.

PUBLICATIONS (Continued)

In lay journals:

1. "Death takes a holiday," Purdue Scientists, 1 , 9-11 (1947);
2. "How to hunt whitetail deer," Hunting and Fishing, Dec., 58-60 (1947);
3. "The man behind the Nobel prize," Purdue Scientist, 1 , 14-16 (1948);
4. "Recent developments in the field of antidiabetic drugs," The Pennsylvania Pharmacist, 32, 16-33 (1951);

Abstracts of scientific papers:

1. Mann, David E., Jr., and Hiestand, W.A., "The relative antidotal effects of certain organic compounds and potassium cyanide in the albino mouse, "ANATOMICAL RECORD, 101 , 744 (1948);
2. Mann, David E., Jr., Zupko, A.G., Hammond, P.V., and Rockhold, W.T., "The effects of Veratrum viride on the blood sugar level of the albino rat," ANATOMICAL RECORD, 105 , 617 (1949);
3. Mann, David E., Jr., Zupko, A.G., Hammond, P.V., and Rockhold, W.T., "The effects of Veratrum viride on the blood sugar level of the albino rat," Proceedings of the Indiana Academy of Science, 59 ,(1950);
4. Mann, David E., Jr., and Zarrow, M.X., "Normal blood sugars in sheep and lambs," Federation Proceedings, 9 , 84 (1950);
5. Mann, DAvid E., Jr., and Hiestand, W.A., "Alloxan response following prolonged oral administration of thiourea in the rat," ANATOMICAL RECORD , 111 , 578 (1951);
6. Mann, David E., Jr. , "Effect of potassium iodide and potassium iodate on blood sugar response to thiourea, " Journal of Pharmacology and Experimental Therapeutics, 110 , 34 (1954);
7. Swanson, Jr., E. A. , Ploumis, E., and Mann, David E., Jr., "Radiologic and histologic changes in the dental pulp chamber incident to experimental arteriosclerosis," American Journal of Anatomy (accepted for entry), May, 1973.

Journal Articles (Continued) :

20. Kasirsky, G., Gautieri, R.F., and Mann, David E., Jr., "Inhibition of cortisone-induced cleft palate in mice by cobaltous chloride, " Journal of Pharmaceutical Sciences , 56 , 1330-1332 (1967);

21. Mann, David E., Jr., Gautieri, R.F., and Kasirsky, G., "Ionic hormonal precursor hypothesis," The Lancet , March 30th , 1968, p. 699;

22. Arcuri, P. A., and Mann, David E., Jr., "Effect of sodium fluoride and/or sodium iodate on blood sugar response to thiopental in the fasted rabbit," Journal of Pharmaceutical Sciences , 58 , 260-261 (1969);

23. Kasirsky, G., Sherman, W.T., Gautieri, R.F., and Mann, David E., Jr., "Cobalt-cortisone interrelationships in the induction and inhibition of cleft palate in mice, " Journal of Pharmaceutical Sciences , 58 , 766-767 (1969);

24. Burke, D.H., and Mann, David E., Jr., "Influence of several autonomic drugs on sodium nitroprusside and oxotremorine-induced hypothermia in immature and mature mice," Journal of Pharmaceutical Sciences , 59 , 1814-1818 (1970);

25. O'Hara , G.P., Mann, David E., Jr., and Gautieri, R.F., "Effect of cobalt chloride and sodium cobaltinitrite on the growth of established epithelial tumors induced by methylcholanthrene," Journal of Pharmaceutical Sciences , 60 , 473-474 (1971);

Temple Dental Alumni Review magazine:

1. "Dental Therapeutics, 2001," by David E. Mann, Jr., (in press).

AUDIO-VISUAL TAPES:

1. "The Ionic Hormonal Precursor Hypothesis," prepared as a 12-minute tape for TV viewing, embodies the experimental concepts backing our original hypothesis that present-day hormones originated from ions in primeval seas. This tape was one of 13 presented before the Sixth International Congress on Pharmacology, July, 1972, in San Francisco.
2. "Prescription Writing," a 9-minute tape prepared for teaching purposes in the dental school. It illustrates the fundamental principles involved in Rx writing.
3. "Use and Abuse of Local Anesthetics," a 30-minute tape which introduces the student of dentistry to the hazards encountered when local anesthetics are improperly used.

Curriculum Vitae

Name: Robert L. Pollack
Address
Home Telephone Number: REDACTED
Born: Philadelphia, Pa.
Marital Status: REDACTED
Military Experience: Hospital Corps, United States Navy, 1944-45

Education:

B.Sc. in Chemistry, R Philadelphia College of Pharmacy and Science
B.Sc. in Bacteriology, R Phila. College of Pharmacy and Science
M.Sc. in Bacteriology, R Phila. College of Pharmacy and Science
Ph.D. in Biochemistry, R University of Tennessee Medical Units Division, Memphis, Tenn.

Professional Experience:

Professor of Biochemistry and Chairman, Department of Biochemistry and Nutrition, Temple University School of Dentistry, 1962-present.
Consultant in Dental Biochemistry to the Veterans Administration Hospital, Philadelphia, 1962-1967
Senior Research Scientist, Eastern Regional Research Laboratories, U.S. Dept. of Agriculture, Wyndmoor, Pa., 1954-1962.
Adjunct Instructor in Chemistry, Drexel Institute of Technology Evening Division, 1957-1962

Memberships:

REDACTED

Listings in Professional Directories:

American Men in Science
Leaders in American Science
Dictionary of International Biography
Who's Who in American Education

Abstracts Presented at Meetings

1. An Amino acid-steroid conjugate excreted in urine. C.H. Eades, Jr., R.L. Pollack, and J.S. King, Jr., Federation Proc. 13, 201-202 (1954).

2. Respiratory activity of normal and bruised red tart cherry (Prunus cerasus). R.L. Pollack and C.H. Hills, Federation Proc. 15, 328 (1956).

3. Stabilizing apple cider by mild heat treatment. J.F. Robinson, R.L. Pollack, and C.H. Hills. 18th annula meeting, Institute of Food Technologists. Chicago, Ill. 1958.

4. The respiratory activity of the red tart cherry during growth. Robert L. Pollack and Claude H. Hills. IXth International Botanical Congress, Montreal, Canada, August, 1959.

5. A quantitative study of the nitrogenous components of the red tart cherry. R.M. Zacharius and R.L. Pollack. Oregon State University. Corvalis, Oregon, 1962.

6. The respiratory activity of lathrogen-treated strain "L" fibroblasts in culture. J.J. Aleo, R.L. Pollack, and G.R. Schacterle. 45th General Meeting, International Assoc. for Dental Research, March, 1967.

7. Substrate and cofactor effects on respiration of bovine dental pulp. R. L. Pollack, D. Green, and T. Rosett, 49th general meeting of the International Association for Dental Research, March, 1971.

8. Model systems for the study of oral tissue; gingival and lingual epithelium and dental pulp. T. Rosett, L. P. Gangarosa, R. L. Pollack, D. Green, and P. Garner. 55th annual meeting of the Federation of American Societies for Experimental Biology, April, 1971.

9. An individualized instruction procedure for a biochemistry laboratory experiment. T. Rosett and R. L. Pollack. Section on Learning Resources, American Association of Dental Schools, March, 1972.

Robert L. Pollack
Curriculum vitae

Publications

1. Determination of Free and Combined Amino Acids in Urine, Robert L. Pollack and C.H. Eades, Jr., Anal. Chem. 24, 2017 (1952).

2. Glucuronic Acid Conjugates of Aspartic and Glutamic Acids in Urine, Robert L. Pollack, and C.H. Eades, Jr., Science 119, 510-511 (1954).

3. Urinary Excretion of Fourteen Amino Acids by Normal and Cancer Subjects, C.H. Eades, Jr., and Robert L. Pollack, J. National Cancer Institute 15, 421-427 (1954).

4. Thermal Burns in Man. IX. Urinary Amino Acid Patterns, Charles H. Eades, Jr., Robert L. Pollack, and James D. Hardy, J. Clinical Investigation, 34, 1756-1759 (1955).

5. Studies on Cherry Scald. I. Relationship Between Bruising and Respiration in Water, Robert L. Pollack, C. Ricciuti, C.F. Woodward, and C.H. Hills, Food Tech. 12, 102-105 (1958).

6. Studies on Cherry Scald. II. Relationship Between Bruising and Respiration in Air. Robert L. Pollack, Claude H. Hills and R.T. Wittenberger, Food Tech. 12, 106-108 (1958).

7. A Rapid Method for Serum Uric Acid without Cyanide, G.F. Grossman, A. Grossman, E. Kravitz and R. L. Rollack, American Journal of Pharmacy 133, 213-218, 1961.

8. Respiratory Activity of the Red Tart Cherry (Prunus Cerasus) During Growth. Robert L. Pollack, Nancy Hoban, and Claude H. Hills, Proc. Am. Soc. Hort. Sci., 78, 86-95, 1961.

9. Self Mountable Support - U.S. Patent Application #270084. Filed April 2, 1963. Issued, August 24, 1965.

10. Modifications to the Autoanalyzer for the rapid recording of optical densities. A. Grossman, G.F. Groossman, R.L. Pollack, and E. Kravitz, Anal. Biochem. 8, 124-126, 1964.

11. Respiration in bruised fruit tissue. Robert L. Pollack, Grafton C. Chase, and Joseph L. Rabinowitz, Atompraxis 11, Sept/Oct., 562-564, 1965.

12. Effect of Bruising and Aging on the Alcohol-Insoluble Solids of Red Tart Cherries. R.H. Golder, S.M.Levin, G. R. Schacterle, and R.L. Pollack. J. Agric. & Food Chem. 20, 680,1972.

13. The Comparative Analysis of Diabetic and Non-Diabetic Saliva. Protein separation by disc gel electrophoresis. A.J.Finestone, G.R.Schacterle, and R. L.Pollack. Accepted for publication by the Journal of Periodontology.

14. Respiration of homogenates and crude mitochondrial fractions of bovine attached gingiva. T. Rosett, L.P. Gangarosa, E.L. Ashbridge, A. Belsky, G. Derenzo, H. Elder, R.L.Pollack, U. Sacco, and N. Tan. Archs. Oral Biol. 17,1543-1550, 1972.

15. Respiration of homogenates and mitochondrial fractions of bovine dental pulp. T. Rosett, E. Ashbridge, A. Belsky, G. Derenzo, P.S. Garner, D. Green, R.L.Pollack, and N. Tan. Archs. Oral Biol. 17, 1691-1698, 1972.

16. A Simplified Method for the Quantitative Assay of Small Amounts of Protein in Biologic Material. G.R. Schacterle and R. L. Pollack, Accepted for publication in Analytical Biochemistry.